Notice of Allowability	Application No.	Applicant(s)	
	10/646,664	SHEN ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *10/22/07*.

2. ☒ The allowed claim(s) is/are *1-18 and 21-25*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

1. Claims 1-25 are pending.

Applicants' amendment filed January 26, 2007 and Applicants' supplemental appeal Brief filed October 22, 2007 are acknowledged. Applicants' response has been fully considered. In the amendment, claims 1-18 and 21-25 have been amended. Claims 19 and 20 are non-elected invention and withdrawn from consideration. Therefore, claims 1-18 and 21-25 are examined.

Withdrawn Claim Rejections -35 USC § 112

2. The previous rejection of claims 1-18 and 21-25 under 35 U.S.C. 112, first paragraph, scope of enablement, is withdrawn in view of applicants' response at pages 6-8 in the supplemental appeal Brief filed October 22, 2007, and Examiner's amendment (see below).

3. The previous rejection of claims 1-18 and 21-25 under 35 U.S.C. 112, first paragraph, written description, is withdrawn in view of applicants' response at pages 8-9 in the supplemental appeal Brief filed October 22, 2007, and Examiner's amendment (see below).

4. The previous rejection of claims 9, 10-16 and 17-18 under 35 U.S.C. 112, second paragraph is withdrawn in view of applicants' response at page 9 in the amendment filed January 26, 2007, and Examiner's amendment (see below).

Examiner's Amendment

An **Examiner's Amendment** to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Steven Highlander on December 17, 2007.

Examiner's Amendments to the Claims:

Cancel claims 19 and 20.

Claims 1-3, 9, 10, 16-18, 21, 23 and 25 have been amended as follows.

1. (Currently amended) A method of modifying a biological molecule by formation of a ~~C--O~~ C-O bond comprising the step of contacting a biological molecule with a polypeptide selected from the group consisting of: (a) a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 3; (b) a polypeptide encoded by a nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO: 2; and (c) a polypeptide encoded by a nucleic acid that specifically hybridizes ~~under highly stringent conditions~~ to SEQ ID NO: 2 under wash conditions of at least as stringent as 0.2 x SSC wash at 65 °C for 15 minutes and which catalyzes ~~C--O~~ C-O bond formation; wherein said biological molecule is a substrate for said polypeptide, and whereby said polypeptide modifies the biological molecule by formation of a ~~C--O~~ C-O bond.

2. (Currently amended) The method according to claim 1, further comprising the step of contacting the biological molecule modified by the polypeptide recited in claim 1 with a second polypeptide selected from the group consisting of: (a) a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 5; (b) a polypeptide encoded by a nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO: 4; and (c) a polypeptide encoded by a nucleic acid that specifically hybridizes ~~under moderately stringent conditions~~ to SEQ ID NO: 4 under wash conditions of at least as stringent as 0.2 x SSC wash at 65 °C for 15 minutes and which catalyzes ~~C--O~~ C-O bond formation; whereby said second polypeptide further modifies the biological molecule by formation of a ~~C--O~~ C-O bond.

3. (Currently amended) The method according to claim 1, wherein the ~~C--O~~ C-O bond formed is between the biological molecule and a second biological molecule, said second biological molecule being also a substrate for the polypeptide.

9. (Currently amended) The method according to claim 1, wherein said biological molecule is an enantiomeric ~~nonactin or analog thereof~~ nonactic acid compound.

10. (Currently amended) A method of catalyzing a ~~C—O~~ C-O bond formation between biological molecules comprising the step of contacting biological molecules with at least one polypeptide encoded by a nucleic acid comprising the sequence set forth in SEQ ID NO: 1, or by a nucleic acid hybridizing to the nucleotide sequence of SEQ ID NO: 1 under ~~stringent~~ wash conditions ~~thereto~~ of at least as stringent as 0.2 x SSC wash at 65 °C for 15 minutes, said biological molecules being substrates for said at least one polypeptide, whereby said at least one polypeptide catalyzes ~~C—O~~ C-O bond formation between the biological molecules.

16. (Currently amended) The method according to claim 10, wherein said biological molecule is an enantiomeric ~~nonactin or analog thereof~~ nonactic acid compound.

17. (Currently amended) A method of producing a macrotetralide or a macrotetralide analogue comprising the steps of (i) contacting enantiomeric ~~nonactins or analogs thereof~~ nonactic acid compounds with at least one polypeptide selected from the group consisting of: (a) a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 3 or 5; (b) a polypeptide encoded by a nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO: 2 or 4; and (c) a polypeptide encoded by a nucleic acid that specifically hybridizes ~~under very stringent conditions~~ to SEQ ID NO: 2 or 4 under wash conditions of at least as stringent as 0.2 x SSC wash at 65 °C for 15 minutes and which catalyzes ~~C—O~~ C-O bond formation; under conditions such that the polypeptide catalyzes ~~C—O~~ C-O bond formation between the enantiomeric ~~nonactins or analogs thereof~~ nonactic acid compounds, whereby a macrotetralide or macrotetralide analogue is thereby synthesized; and (ii) recovering said macrotetralide or macrotetralide analogue.

18. (Currently amended) The method according to claim 17, wherein said method is carried out in a host cell and the enantiomeric ~~nonactins or analogs thereof~~ nonactic acid compounds are exogenously supplied.

21. (Currently amended) A method of catalyzing ~~C—O~~ C-O bond formation between biological molecules comprising the step of contacting biological molecules with a polypeptide selected from the group consisting of: (a) a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 3; (b) a polypeptide encoded by a nucleic acid comprising the nucleotide

sequence set forth in SEQ ID NO: 2; and (c) a polypeptide encoded by a nucleic acid that specifically hybridizes ~~under very stringent conditions~~ to SEQ ID NO: 2 under wash conditions of at least as stringent as 0.2 x SSC wash at 65 °C for 15 minutes and which catalyzes ~~C—O~~ C-O bond formation; wherein said biological molecules are substrates for said polypeptide, whereby said polypeptide catalyzes ~~C—O~~ C-O bond formation between the biological molecules.

23. (Currently amended) A method of catalyzing ~~C—O~~ C-O bond formation between biological molecules comprising the step of contacting biological molecules with a polypeptide selected from the group consisting of: (a) a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 5; (b) a polypeptide encoded by a nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO: 4; and (c) a polypeptide encoded by a nucleic acid that specifically hybridizes ~~under moderately stringent conditions~~ to SEQ ID NO: 4 under wash conditions of at least as stringent as 0.2 x SSC wash at 65 °C for 15 minutes and which catalyzes ~~C—O~~ C-O bond formation; wherein said biological molecules are substrates for said polypeptide, whereby said polypeptide catalyzes ~~C—O~~ C-O bond formation between the biological molecules.

25. (Currently amended) A method of ~~chemically~~ modifying a biological molecule by formation of a ~~C—O~~ C-O bond comprising contacting a biological molecule with a polypeptide selected from the group consisting of: (a) a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 3 or 5; (b) a polypeptide encoded by a nucleic acid comprising the nucleotide sequence consisting of SEQ ID NO: 2 or 4; and (c) a polypeptide encoded by a nucleic acid that specifically hybridizes ~~under moderately stringent conditions~~ to SEQ ID NO: 2 or 4 under wash conditions of at least as stringent as 0.2 x SSC wash at 65 °C for 15 minutes and which catalyzes C-O bond formation; wherein said biological molecules is a substrate for said polypeptide, whereby said polypeptide ~~chemically~~ modifies the biological molecule by formation of a ~~C—O~~ C-O bond.

The following is an **Examiner's Statement of Reasons for Allowance**:

The following reference appears to be the closest art to the claimed invention. Walczak et al. (FEMS Microbiology Letters 183, 171-175 (2000)) teach the isolation and sequencing of 15559 bp of chromosomal DNA of nonactin biosynthsis gene cluster from S. grieseus, and indicates two of the genes, NonK and NonJ are unusual ketoacyl synthase (KAS)α and KASβ

homologues. However, the reference does not teach using the polypeptide encoded by the NonK and/or NonJ genes to catalyze a C-O bond formation in a method of modifying a biological molecule by formation of a C-O bond, a method of catalyzing a C-O bond between biological molecules, or a method of producing a macrotetralide. Therefore, the claims are allowable over the art of record.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Bragdon can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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CMK
December 18, 2007